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Case Report

Hepatitis Induced by Anti-Tubercular Therapy and Chronic Alcoholism: A Case Report

Rohit Bangwal¹, Yogesh Joshi^{1*}, Jagdish Rawat²

1. Department of Pharmacy Practice, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Dehradun-248001, Uttarakhand (India)
2. Department of Pulmonary Medicine, Shri Guru Ram Rai Institute of Medical & Health Sciences, Patel Nagar, Dehradun-248001, Uttarakhand (India)

ABSTRACT

Anti-tubercular drugs induced hepatotoxicity, which is a serious problem and it was reported that worldwide 2-32% of TB patients experience drug induced hepatotoxicity (DIH) during the course of the treatment. A 65 year old male, 47 kg weight and chronic alcoholic was brought to a tertiary care hospital in semi-conscious condition with chief complains of vomiting, cough with expectoration, loss of appetite, shortness of breath, fever (on & off) since 4 days. He had a history of smear positive pulmonary koch's 10 days back and was taking regular first line anti-tubercular drug therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol). In this case, the patient was also chronic alcohol consumer and a known case of chronic obstructive pulmonary disease (COPD) since 2 years. After 10 days of anti-tubercular drug therapy, patient was found to develop hepatotoxicity with the findings of elevated total bilirubin and liver enzymes level. Viral markers for hepatitis, including hepatitis B viruses (HBV), hepatitis C viruses (HCV), human immunodeficiency virus (HIV), were all are non-reactive. Physician found provisional diagnosis of anti-tubercular drugs with alcohol induced hepatitis. Patient was on hold of previous anti-tubercular drugs therapy. Although it was started modified anti-tubercular drugs (Streptomycin, Levofloxacin, Ethambutol) therapy along with liver tonics. Upon normalization of patient conditions, physician started first line anti-tubercular drug therapy containing Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and Pyridoxine with continued liver tonics. Routine monitoring of liver enzymes, total bilirubin were followed up till discharged. Such type of case studies with confirmed pulmonary koch's conditions suggested to follow alcohol withdrawal with standard treatment and standard care to achieve a favorable outcome.

Keywords: Anti-tubercular drugs, adverse effects, hepatotoxicity, liver enzymes, alcoholism

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*Address for Correspondence:

Yogesh Joshi, Department of Pharmacy Practice, School of Pharmaceutical Sciences, Shri Guru Ram Rai University, Dehradun-248001, Uttarakhand (India)

INTRODUCTION

As per world health organization (WHO), tuberculosis (TB) is affecting one third of the population worldwide and one out of four adult male deaths is attributed to TB^{1,2}. The first line anti-TB drugs have the potentiality to cause hepatotoxicity. From first line anti-TB drugs, isoniazid (INH), rifampin (RIF), and pyrazinamide (PZA) causes hepatotoxicity²⁻⁵. The risk factors for anti-TB induced hepatotoxicity includes high alcohol intake, older age, pre-existing chronic liver disease, chronic viral infection due to hepatitis B (HBV) and hepatitis C viruses (HCV), human immunodeficiency virus (HIV) infection, advanced TB, Asian ethnicity, concomitant administration of enzyme-inducers, inappropriate use of drugs and poor nutritional status^{2,6,7}.

Tuberculosis and chronic obstructive pulmonary disease (COPD) are two important causes of mortality and morbidity in our country and are among top 10 causes of death. The interrelationship between TB and COPD is very complex. A substantial number of TB patients develop post-tubercular airway disease or TB-associated COPD. Although tuberculosis is a curable disease, it continues to be one of the leading infections associated with death in the world. The incidence rate of anti-tubercular drugs induced hepatotoxicity in India was found to be 2% to 28%^{6,8}. COPD patients are also at high risk of developing pulmonary TB. COPD is a second most common comorbidity in patients with TB after diabetes. History of TB negatively impacts the long-term course of COPD with early mortality and increased frequency of exacerbations. COPD also alters the clinical

presentation of TB and is a risk factor for increased morbidity and mortality from TB⁹⁻¹¹.

CASE REPORT

- ❖ In this case report 65 year old male, weighing 47 kg, admitted to pulmonary ward of shri mahant indresh hospital, Dehradun with chief complains of vomiting, cough with expectoration, loss of appetite, shortness of breath, fever (on & off) since 4 days. The patient was chronic alcoholic and consumed large amounts of alcohol with ATT drugs which may leads to changes liver conditions. He had a history of smear positive pulmonary koch's 10 days back and was taking regular first line anti-tubercular drug therapy (Isoniazid, Rifampicin, Pyrazinamide and Ethambutol). On the same day, pulmonologist prescribed the following drugs to the patient after examination:
 1. Tablet Levocetirizine - 5mg HS
 2. Tablet Methyl Prednisolone -16mg BD
 3. Injection Pantoprazole - 40mg OD
 4. Tablet Hepamerz (L-Ornithine + L-Aspartate) 5mg (1Tab) BD
 5. Syrup Liv-52 2tsf TDS
 6. Nebulization
 7. 2 bottle normal saline i.v. - 100ml/hour
 8. Hold the CAT 1st ATT medication therapy.
- ❖ On the 2nd day, alcoholic withdrawal symptoms such as delirium were seen in the patient. Blood pressure was recorded as 110/70 mmHg and pulse rate was 61/min. The patient was prescribed with injection Diazepam 5mg in 10ml normal saline and start the modified anti-tubercular therapy (levofloxacin 750mg OD, ethambutol 800mg OD, streptomycin 0.75g I/M OD), rest of the treatment was continued.
- ❖ On the 3rd day, patient complaint of anxiety, so prescribed with tablet Lonazepam 0.25mg for 5 days. Blood pressure was normal i.e. 120/70 mmHg and pulse rate was 16/min with SPO₂ concentration 99.2%.
- ❖ On the 4th day, nutritional assessment was done and the patient was on soft liquid food, moderate protein and low fat liquid and same treatment was continued.
- ❖ On 5th day, no fresh complaints were seen and temperature was normal, blood pressure was 110/80, respiratory rate was 20/min, pulse rate was 101/min with SPO₂ concentration 98%. All liver function tests (LFT) reports were found normal. Patient was considered to be the case of Alcoholic liver disease (ALD) with hepatitis.
- ❖ On 6th day, the patient was finally diagnosed as the case of anti-tubercular drug induced hepatitis.
- ❖ On 7th day, physician stopped the modified ATT therapy, and started the CAT 1st DOTS Therapy (Isoniazid, Rifampicin, Pyrazinamide, Ethambutol and Pyridoxine) with proper monitoring of routine LFT investigation.
- ❖ The results of investigations were showed in Table-1.

Table 1: Laboratory Investigation

S.No.	Parameter	Test value (Day-1)	Test value (Last Day)	Normal value
1.	SGOT	712	58	17-59 IU/L
2.	SGPT	868	85	9-52 IU/L
3.	GGT	435	66	12-43 IU/L
4.	Total Bilirubin	2.2	1.4	0.2-1.3 mg/dl
5.	Direct Bilirubin	1.4	0.9	0.0-0.8 mg/dl
6.	ALP	295	76	38-126 IU/L
7.	PT	15	13	9.5-13.5 sec

- ❖ On 8th day, patient was with no fresh complaints and plan for discharge was made.
- ❖ On 9th day, patient was discharge with appropriate medication chart and patient counselling. The discharge medication includes:
 - ✓ Tablet Isoniazid 300mg OD - 1 week
 - ✓ Tablet Rifampin 450mg OD - 1 week
 - ✓ Tablet Ethambutol 800mg OD 1 week
 - ✓ Tablet Pyrazinamide 1200mg OD 1 week
 - ✓ Tablet Pyridoxine 40 mg ½ tab OD (HS) 1 week
 - ✓ Syrup Liv-52 2 tsf TDS
 - ✓ Tab Pantoprazole 40 mg OD
- ✓ Review after 14 days in OPD with the LFT reports

DISCUSSION

Anti-TB drugs induced hepatotoxicity is a serious problem and it was reported that 2-28% of TB patients experience drug related hepatotoxicity (DIH) during the course of the treatment. The incidence rate of drug induced hepatotoxicity in India is 8-36%. The higher incidence of DIH was found in the Asian countries which may be due to ethnic susceptibility, inherent peculiarity of drug metabolism and/or the presence of various known risk factors such as HBV infection, malnutrition, and alcoholism. According to a study, overall incidence of serious adverse effects was three times higher with pyrazinamide than with isoniazide, or rifampicin. Alcoholism is one of the main risk factor which aggravates the anti-TB induced hepatotoxicity. In this case, the patient

was chronic alcoholic and consumed large amounts of alcohol which may lead to following liver conditions - fatty liver, hepatitis and cirrhosis. In this case, hepatitis was seen in the patient. For all types of liver disease caused by alcohol, the main treatment is to stop consumption of alcohol completely. In our case, on withdrawal of alcohol the patient developed alcohol withdrawal syndrome such as delirium and the patient which was treated. Nutritional assessment was done and patient was on soft liquid food, moderate protein and low fat liquid during the course of the treatment. Taking all the information under consideration, a causality assessment of the entitled medical conditions was done by using Naranjo Causality Assessment Algorithm and the results indicated Antitubercular drugs and alcohol as possible cause hepatotoxicity. Upon normalization of patient conditions, physician restarted first line anti-tubercular drug therapy containing Rifampicin, Isoniazid, Pyrazinamide and Ethambutol with continued liver tonics. Routine monitoring of liver enzymes, total bilirubin were followed up till discharged. Upon discharge, patient was counseled regarding the medications and course of the treatment.

CONCLUSION

Patient developed hepatotoxicity and severe alcohol induced hepatitis following the administration of 1st line anti-TB drugs, which were administered for the treatment of pulmonary koch's. Following the withdrawal of alcohol, standard treatment and standard care, we were able to achieve a favorable outcome. As a clinical pharmacist and clinicians are need to be made aware of these potentially fatal adverse effects associated with anti-tubercular therapy via conduction of quality based seminars, conferences, published medical literature and learning programmes and health care camps. We needs and overcome the ATT induced hepatotoxicity by the following programmes like conduction of quality based seminars, health care camps, conferences, published medical literature and learning programmes.

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